UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,261	03/07/2001	David McElroy	950.044US1	5526

7590 11/05/2002

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402

EXAMINER	
FOX, DAVID T	

ART UNIT	PAPER NUMBER
1638	9

DATE MAILED: 11/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/801,261	McElroy et al
Examiner	**Group Art Unit**
FOX	1638

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE -3- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- [x] Responsive to communication(s) filed on 8/9/02.
- [ ] This action is **FINAL.**
- [ ] Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

- [x] Claim(s) 1-51 is/are pending in the application.
  - Of the above claim(s) 1,3-7,22-27,30-51 is/are withdrawn from consideration.
- [ ] Claim(s) _____ is/are allowed.
- [x] Claim(s) 2,8-21,28-29 is/are rejected.
- [ ] Claim(s) _____ is/are objected to.
- [ ] Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- [ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- [ ] The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.
- [ ] The specification is objected to by the Examiner.
- [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- [ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).
  - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
  - ☐ received.
  - ☐ received in Application No. (Series Code/Serial Number) _____.
  - ☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

- [x] Information Disclosure Statement(s), PTO-1449, Paper No(s). 5
- [ ] Interview Summary, PTO-413
- [x] Notice of Reference(s) Cited, PTO-892
- [ ] Notice of Informal Patent Application, PTO-152
- [ ] Notice of Draftsperson's Patent Drawing Review, PTO-948
- [ ] Other _____

Office Action Summary

Applicant's election of Group II in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 2, 8-21 and 28-29 are being examined. Claim 2 is objected to for depending upon non-elected claim 1.

The effective filing date for the instantly claimed invention is 9 March 2000, the filing date of the parent application.

The specification is objected to for its inclusion of active hyperlinks on page 32, line 26. Internet retrieval of any patent issued from the instant specification would result in the incorporation of a live web link within the text of the patent. Since the U.S. Patent and Trademark Office exercises no control over any commercial organization accessible by said hyperlink, USPTO policy does not permit the PTO to link to any commercial sites. Applicants are requested to delete the hyperlinks on page 32.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 8-21 and 28-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-10 of copending Application No. 09/521,557. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill in the art to utilize the direct repeat-mediated method of transgene alteration claimed in the copending application to obtain the direct repeat-mediated method of transgene alteration claimed in the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 8-21 and 28-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to a direct repeat-mediated method for transgene deletion, does not reasonably provide enablement for claims broadly drawn to a direct repeat-mediated method for any type of transgene alteration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification only demonstrates the use of DNA constructs comprising direct repeats to delete transgene portions following recombination, said direct repeats comprising a single

promoter region, the CaMV 35S promoter, and a single intron, the hsp70 intron. No guidance is provided regarding any other type of transgene alteration, such as amplification or rearrangement. In addition, no guidance is provided regarding the development or evaluation of any other type of directly repeating sequences. In contrast, the claims are broadly drawn to any type of transgene alteration, and to any sequence to be used as the direct repeat.

Transgene alteration via recombination between repeated sequences is unpredictable. Zubko et al teach that homologous recombination frequencies are low; that some portions of the transgene not intended to be deleted, i.e. those outside of the region flanked by the direct repeats, were in fact deleted as well; and that the majority of plants transformed with DNA constructs comprising direct repeats did not show any recombination (see, e.g., page 442, column 2, first full paragraph; page 443, Figure 1 and bottom paragraph of column 2; page 444, column 2, second full paragraph). Conner et al teach that environmental fluctuations can exert a strong influence on loss of marker gene expression (see, e.g., page 53, column 2), wherein said fluctuations would confound the evaluation of transgene loss due to recombination between directly repeated sequences.

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for effecting a multitude of types of transgene alterations following recombination between directly repeated sequences having a multitude of different sequences, particularly wherein desired (i.e. non-antibiotic resistance marker gene) portions of the transgene are not lost.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is indefinite in its recitation of "the progeny transgenic plant cell of claim 1" which lacks antecedent basis, since claim 1 is not drawn to a plant cell.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 2, 8-15, 19, 21 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Conner et al.

Conner et al teach tobacco plant transformation with a transgene insertion comprising an nptII gene conferring kanamycin resistance and a GUS gene, flanked by directly repeating matrix associated regions; wherein the resultant transgenic plants were self-pollinated to generate progeny or outcrossed to wild-type plants to obtain progeny; and wherein progeny were selected with transgene alterations as evidenced by kanamycin sensitivity and lack of GUS production (see,

e.g., page 48, column 2, middle paragraph; page 49, Figure 1 and top paragraph of column 1; page 50, column 2, top paragraph; page 52, Figure 2C and column 2; page 56, column 2).

Claims 2, 8-13, 15, 19, 21 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Assaad et al.

Assaad et al teach a method of transforming Arabidopsis plants with a transgene insertion comprising a pre-selected hygromycin phosphotransferase DNA sequence conferring hygromycin resistance, flanked by directly repeated portions of an nptII gene conferring resistance to kanamycin; obtaining progeny of the transformed hygromycin resistant plants via self-pollination; and selecting fertile transgenic progeny with an altered transgene insertion as evidenced by their hygromycin sensitivity (see, e.g., page 554, column 1, bottom paragraph, column 2, top three paragraphs; page 555, Figure 1 and first full paragraph of column 1, column 2, bottom paragraph; page 556, Table 1 and paragraph bridging the columns; page 557, column 2, penultimate paragraph; page 558, Figure 3; page 560, Figure 5; page 561, Table 3, especially rows designated as "NR9", "NR14", "NR21" and "NR29").

Claims 2, 8-13, 15, 19, 21 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Swoboda et al (1994).

Swoboda et al (1994) teach a method of transforming Arabidopsis plants with a transgene insertion comprising a pre-selected hygromycin phosphotransferase DNA sequence conferring hygromycin resistance, flanked by directly repeated portions of a GUS gene; obtaining progeny of the transformed hygromycin resistant plants via self-pollination; and selecting fertile transgenic

progeny with an altered transgene insertion as evidenced by their hygromycin sensitivity and GUS production (see, e.g., page 484, column 2, penultimate paragraph; page 485, Figure 1; page 486, Figure 2; page 487, paragraph bridging the columns; page 488, column 2, second and third full paragraphs).

Claims 2, 8-11, 13-15, 19, 21 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Odell et al (U.S. Patent 5,658,772).

Odell et al teach a method for preparing a fertile transgenic tobacco plant having an altered transgene insertion, said altered transgene insertion comprising deletion of the selectable marker gene (conferring herbicide resistance) necessary for initial transformant selection but undesired in the final product, said method comprising obtaining a first fertile transgenic plant which has been selfed to be homozygous for a trangene insertion sequence comprising a pre-selected DNA sequence comprising a mutant ALS marker gene and flanked by directly repeating lox sequences, obtaining a plurality of progeny of said first transgenic plant via self-pollination, and then crossing with another plant containing a cre gene to obtain progeny with an altered transgene insertion, namely deletion of the selectable marker gene (see, e.g., Figure 4; column 2, lines 40-67; column 3, lines 1-7; column 4, lines 15-28; paragraph bridging columns 5 and 6; paragraph bridging columns 8 and 9; column 10, lines 1-5; column 15, line 48 through line 67 of column 16; column 31, line 40 through line 10 of column 37).

Claims 2, 8-12, 14, 19, 21 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/13401 (PURDUE).

PURDUE teaches a method for producing a fertile transgenic dicotylodenous *Arabidopsis* plant having an altered transgene insertion, said method comprising obtaining a first female fertile transgenic plant homozygous for a transgene insertion sequence comprising a suicide gene and a selectable *bar* gene flanked by directly repeating FRT sequences, said method further comprising outcrossing said female fertile transgenic plant to a wild-type plant comprising a FLP gene, wherein fertile progeny not comprising the *bar* gene are produced (see, e.g., Figures 1a, 2, 3 and 5b; page 1, bottom paragraph; page 3, line 3 through page 4, line 1; page 4, line 19 through page 5, line 6; page 8, line 27 through page 9, line 29; page 12, lines 10-27; page 13, lines 21-26; page 34, line 27 through page 36, line 17; page 37, line 23 through page 38, line 22).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 8-18, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Odell et al (U.S. Patent 5,658,772) taken with D'Halluin et al.

Odell et al teach a method for preparing a fertile transgenic plant with an altered transgene insertion in order to subsequently delete undesired marker genes as discussed above, but do not teach the use of the *bar*, *nptII* or *cryIA(b)* genes as the portion of the transgene to be altered, and do not teach whole cereal plants containing said altered transgene.

Odell et al suggest the use of a variety of transformation techniques including electroporation and other means of direct gene transfer (see, e.g., paragraph bridging columns 5 and 6). Odell et al also teach the use of the *nptII* marker gene for the selection of transformants (see, e.g., Figures 1C, and 2A-2C).

D'Halluin et al teach an electroporation-mediated method for obtaining fertile transgenic maize plants, wherein said method is advantageous for introducing heterologous genes of interest into a wide variety of agronomically desirable maize genotypes (see, e.g., page 1495, column 1, first paragraph of "Introduction", column 2; page 1496; page 1499; page 1503, column 1, middle two paragraphs).

It would have been obvious to one of ordinary skill in the art to utilize the method of transgene alteration to delete undesired marker genes as taught by Odell et al, and to modify that method by utilizing electroporation of the agronomically important crop of maize as taught by D'Halluin et al, as suggested by each reference. Choice of known marker gene to be excised, or choice of self- or cross-pollination to propagate progeny and obtain true-breeding inbred lines,

would have been the optimization of process parameters well known to those of ordinary skill in the art.

Claims 2, 8-18, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/13401 (PURDUE) taken with D'Halluin et al.

PURDUE teach a method for preparing a fertile transgenic plant with an altered transgene insertion in order to subsequently delete undesired genes as discussed above, but do not teach whole cereal plants containing said altered transgene.

PURDUE also summarizes the availability of several transformation methods including electroporation, and teach the transformation of maize protoplasts with a DNA construct comprising a GUS gene flanked by an *nptII* marker gene and two directly repeated FRT sequences, wherein introduction of a FLP gene resulted in excision of the *nptII* gene in transformed callus grown from the transformed protoplasts (see, e.g., page 17, line 29 through page 18, line 13; page 29; page 31, line 23 through page 33, line 3).

D'Halluin et al teach an electroporation-mediated method for obtaining fertile transgenic maize plants, wherein said method is advantageous for introducing heterologous genes of interest into a wide variety of agronomically desirable maize genotypes (see, e.g., page 1495, column 1, first paragraph of "Introduction", column 2; page 1496; page 1499; page 1503, column 1, middle two paragraphs).

It would have been obvious to one of ordinary skill in the art to utilize the method of transgene alteration to delete undesired marker genes as taught by PURDUE, and to modify that

method by utilizing electroporation of the agronomically important crop of maize as taught by D'Halluin et al, as suggested by each reference. Choice of self- or cross-pollination to propagate progeny and obtain true-breeding inbred lines would have been the optimization of process parameters well known to those of ordinary skill in the art.

Claims 2, 8-15, 19-21 and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Odell et al (U.S. 5,658,772) taken with Hinchee et al.

Odell et al teach a method for preparing a fertile transgenic plant with an altered transgene insertion in order to subsequently delete undesired marker genes as discussed above, in particular *Agrobacterium*-mediated transformation of the dicot tobacco, but do not teach the use of the *bar*, *nptII* or *cryIA(b)* genes as the portion of the transgene to be altered, and do not teach whole soybean plants containing said altered transgene.

Odell et al suggest the use of a variety of transformation techniques including electroporation and other means of direct gene transfer (see, e.g., paragraph bridging columns 5 and 6). Odell et al also teach the use of the *nptII* marker gene for the selection of transformants (see, e.g., Figures 1C, and 2A-2C). Odell et al also suggest the use of the technique in plants which are grown for oil (see, e.g., column 10, lines 1-13 and lines 31-36), and mentions soybean as a source of desirable promoters (see, e.g., column 12, lines 43-48).

Hinchee et al teach *Agrobacterium*-mediated soybean transformation, and suggest the broad applicability of the technique to introduce a variety of agronomically desirable transgenes

including those affecting seed oil quality (see, e.g., page 915; page 919, column 2, penultimate paragraph).

It would have been obvious to one of ordinary skill in the art to utilize the Agrobacterium-mediated method of transgene alteration to delete undesired marker genes in dicots as taught by Odell et al, and to modify that method by utilizing electroporation of the agronomically important crop of soybean, as taught by Hinchee et al, as suggested by each reference. Choice of known marker gene to be excised, or choice of self- or cross-pollination to propagate progeny and obtain true-breeding inbred lines, would have been the optimization of process parameters well known to those of ordinary skill in the art.

Claims 2, 8-15, 19, 21 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Selten et al (U.S. 5,876,988 effectively filed July 1994) taken with Lee et al (1990, The Plant Cell).

Selten et al teach the use of eukaryotic fungal or yeast transformation with a selectable marker gene flanked by directly repeating sequences, wherein homologous recombination of said direct repeats result in deletion of the selectable marker gene, wherein said removal of selectable marker genes is environmentally and ecologically advantageous, and also suggests the use of the technique in higher plants (see, e.g., Figures 12a and 12b and Figures 26a-d; column 2, lines 6-12, 23-28, 38-40 and 48-50; column 3, lines 5-16; column 4, lines 22-27 and lines 42-59; column 6, top paragraph; column 7, bottom two paragraphs; column 8, lines 1-5 and 38-53; column 9, lines

5-31; column 11, lines 44-48; column 14, lines 24-63; column 16, lines 40-67; column 19, line 60 through column 20, line 64; column 24 through column 25, line 18).

Selten et al do not actually teach transformed plants.

Lee et al teach the use of gene targeting with an endogenous plant DNA sequence to effect homologous recombination in *Agrobacterium*-mediated transformed dicotyledonous tobacco plants (see, e.g., page 415, Abstract; paragraph bridging pages 415 and 416; page 416, Figure 1; page 417, Figure 2 and column 2).

It would have been obvious to one of ordinary skill in the art to utilize the method of homologous recombination of directly repeated sequences in eukaryotes for the deletion of selectable marker genes as taught by Selten et al, and to modify that method by incorporating the plant transformation techniques of Lee et al, given the suggestion to do so by Selten et al and the demonstration of successful homologous recombination in plants taught by Lee et al. Choice of known marker gene to be excised, or choice of self- or cross-pollination to propagate progeny and obtain true-breeding inbred lines, would have been the optimization of process parameters well known to those of ordinary skill in the art.

Claims 2, 8-15, 19-21 and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Selten et al (U.S. 5,876,988 effectively filed July 1994) taken with Lee et al (1990) and Hinchee et al.

Selten et al (U.S. 5,876,988 effectively filed July 1994) taken with Lee et al (1990) teach a method of homologous recombination of directly repeating flanking sequences to delete selectable marker genes in dicots as stated above, but do not teach soybean transformation.

Hinchee et al teach soybean transformation and suggest the broad applicability of the technique for the introduction of agronomic traits into this important agronomic crop, as stated above.

It would have been obvious to one of ordinary skill in the art to utilize the method of homologous recombination of directly repeating flanking sequences to delete selectable marker genes in dicots as taught by Selten et al taken with Lee et al, and to modify that method by incorporating the soybean transformation technique taught by Hinchee et al, as suggested by Hinchee et al. Choice of known marker gene to be excised, or choice of self- or cross-pollination to propagate progeny and obtain true-breeding inbred lines, would have been the optimization of process parameters well known to those of ordinary skill in the art.

Claims 2, 8-18, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Selten et al (U.S. 5,876,988 effectively filed July 1994) taken with Lee et al (1990) and D'Halluin et al.

Selten et al (U.S. 5,876,988 effectively filed July 1994) taken with Lee et al (1990) teach a method of homologous recombination of directly repeating flanking sequences to delete selectable marker genes in dicots as stated above, but do not teach maize transformation.

D'Halluin et al teach maize transformation, and suggest the broad applicability of the technique to introduce a variety of agronomic traits into this important crop, as stated above.

It would have been obvious to one of ordinary skill in the art to utilize the method of homologous recombination of directly repeating flanking sequences to delete selectable marker genes in dicots as taught by Selten et al taken with Lee et al, and to modify that method by incorporating the maize transformation technique taught by D'Halluin et al, as suggested by D'Halluin et al. Choice of known marker gene to be excised, or choice of self- or cross-pollination to propagate progeny and obtain true-breeding inbred lines, would have been the optimization of process parameters well known to those of ordinary skill in the art.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (703) 308-0280. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (703) 306-3218. The fax phone number for this Group is (703) 872-9306. The after final fax phone number is (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

November 4, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638